

REMARKS

Status of the Claims

Claims pending in the above-identified application are Claims 1-6, 8-14, and 16-34. Applicants recognize that the restriction requirement has been made final, and Claims 8-9 and 16-26 are withdrawn. Claims 1, 3, 4, 6, 10, 12-14, 27, 28, 31, and 34 are amended. The amendments do not introduce new matter into the above-identified application. Support for the amendments is found throughout the specification.

Objection to the Written Description

The U.S. Patent and Trademark Office (PTO) objected to certain informalities in the written description. Certain Greek letters were inadvertently printed as "dots", which one of ordinary skill in the art would readily appreciate as typographical errors. The dots have been replaced with the appropriate symbols known in the art and add no new matter. In view of the above amendments to the written description as suggested by the PTO, Applicants respectfully assert that this objection is obviated. Accordingly, Applicants respectfully request the objection to the written description be withdrawn.

Objection to the Claims

Claims 4, 10, 13, and 24 are objected to because of certain informalities, namely, missing commas. In view of the above amendments to Claims 4, 10, 13, and 24 as suggested by the PTO, Applicants respectfully assert that the objections are obviated. Accordingly, Applicants respectfully request the objections to Claims 4, 10, 13, and 24 be withdrawn.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-6, 10-14, and 27-34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In view of the above amendments and the following remarks, Applicants request that this rejection be withdrawn.

The PTO states that is unclear as to what kind of activity is intended in line 1 of Claim 1. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

In Claim 1, line 4, the PTO asserts that “stimulatory agent” is unclear as to what kind of cell activity or function is intended to be stimulated. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

The PTO asserts that it is not clear in step c) of Claim 1 if the secreted determinant is obtained from the cell culture or from another source. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

In step d) of Claim 1, the PTO asserts that no conclusion is drawn from the “comparing” that relates to the goal set forth in the preamble. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

Similar amendments made to Claim 1 have been made to Claims 10, steps c) – d), and 27, steps b) – d). In view of the above amendments, Applicants respectfully assert that the above referenced rejection is obviated.

The PTO asserts Claims 4, 13, and 28 have improper Markush groups. In view of the above respective amendments, Applicants respectfully assert that this rejection is obviated.

In Claim 14 the PTO states that the phrase “the stimulatory agent” lacks antecedent basis. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

Accordingly, Applicants respectfully request that the rejection of Claims 1-6, 10-14, and 27-34 under 35 U.S.C. § 112, second paragraph, be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 10-14 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In view of the above amendment to Claim 10, Applicants respectfully request this rejection be withdrawn.

The PTO asserts that “[the] assay of claim 10 does not enable the detecting of any composition that ‘affects glycosylated protein accumulation’ as stated in the preamble.” The preamble has been amended to reflect “a method for detecting compositions that affect glycosylated protein.” Additionally, steps a), c), and d) are amended to delete the word

“accumulation”. The claimed method does detect the effect of any composition upon a determinant of a glycated protein produced from the respective cell cultures. As such it is possible to determine the affect of the composition be tested by measuring and comparing the differences in production of the determinant of the glycated protein. In view of the amendment to Claim 10, Applicants respectfully assert that Claims 10-14 are enabled. Accordingly, Applicants respectfully request that the rejection of Claims 10-14 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 1-6, 10-14, and 27-34 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the relevant art to make and/or use the claimed invention. Specifically, in step c) of Claims 1, 10, and 27, respectively, has not been enabled for all of the recited “secreted determinants of inflammation. In view of the above amendments , Applicants request that this rejection be withdrawn.

The PTO states that not all of the recited determinants “can be properly considered as ‘secreted.’” However, all of the recited determinants can be properly consider as being “produced”, which the rejected claimes have been amended to so reflect. In view of the above amendment, Applicants respectfully assert that this rejection is obviated.

Accordingly, Applicants respectfully request that this rejection of Claims 1-6, 10-14, and 27-34 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Rejection Under 35 U.S.C. § 102(b)

Claims 1-6, 10-14, and 27-34 are rejected under 35 U.S.C. § 102(b) as being anticipated by Bian et al. (Curr Eye Res, 12, 439, 1997) (“*Bian*”). Applicants believe that this reference cite is in error and actually should be Curr Eye Res, 17, 65-72, 1998. Respectfully, Applicants request the PTO to enter this correction to the Information Disclosure Statement reviewed by the above referenced Examiner on February 14, 2005, form PTO/SB/08B, date stamped January 21, 2003, cite no. AA. Applicants’ response is in view of the Bian et al.

reference filed in this Information Disclosure Statement. In view of the above amendments, Applicants respectfully assert that this rejection is obviated.

According to the PTO, *Bian* teaches when HCKs are incubated with G-HAS, they secrete IL-8 and MCP-1. Further, the PTO asserts that *Bian* also treats a like cell culture by adding glucose prior to stimulation with the G-HAS and compares IL-8 and CCP-I secretion in cultures with and without addition of glucose.

Actually, *Bian* shows that glycated albumin was only effective in retinal pigment epithelial cells and human corneal keratocytes in inducing inflammatory cytokine (IL-8 and MCP-1) expression. Their data in fact shows in human umbellical vein endothelial cells glycated albumin was **ineffective** in inducing cytokine expression. The present invention employed microvascular and/or aortic endothelial cells, which are more relevant to inflammation, and showed that glycated albumin can induce inflammatory cytokine expression in these endothelial cells. Thus, the data presented in Applicants' disclosure contrast those published by *Bian*. Thus, *Bian* does not teach or suggest a method of detecting the activity of a composition for inhibiting inflammation, as claimed in Claim 1 or any claim depending therefrom. Also, *Bian* does not teach or suggest a method for detecting compositions that affect glycated protein, as claimed in Claim 10 or any claim depending therefrom. Further, *Bian* does not teach or suggest a method for detecting compositions that affect inflammation, as claimed in Claim 27 or any claim depending therefrom.

Accordingly, Applicants respectfully request that the rejection of Claims 1-6, 10-14, and 27-34 under 35 U.S.C. § 102(b) as being anticipated by *Bian* be withdrawn.

Claims 1, 2, 4, 10, 11, 13, 27-29, 32, and 33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Yan et al (PNAS, 94, 5296, 1997) ("*Yan*").

The PTO asserts that *Yan* teaches that when human neuroblastoma cells are incubated with beta amyloid peptide (A. beta), they secrete M-CSF, which corresponds to a "second cell culture". According to the PTO, *Yan* also treat like cell cultures with the addition of cyclohexamide, N-acetylcysteine, or anti-RAGE prior to the addition of the stimulating A. beta. Thus, the PTO concludes that these three additives inhibit the secretion of M-CSF by the neuroblastomice cells.

However, the data presented by *Yan* specifically shows the effects of A. beta in neuronal cells. This study did not address the effects of glycated albumin on cytokine expression in vascular cells. When A. beta binds to neuronal Receptor for Advanced Glycation Endproduct (RAGE), a cell surface receptor for A. beta, it induces macrophage-colony stimulating factor (M-CSF) by an oxidant sensitive, nuclear factor kappaB-dependent pathway. The claimed invention employs vascular and/or aortic endothelial cells. *Yan* is silent with respect to glycated albumin and its effects on inflammatory cytokine expression in endothelial cells. Thus, *Yan* does not teach or suggest the claimed invention.

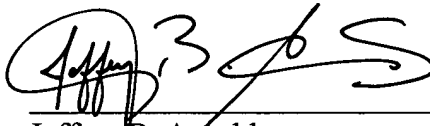
Accordingly, Applicants respectfully request that the rejection of Claims 1, 2, 4, 10, 11, 13, 27-29, 32, and 33 under 35 U.S.C. § 102(b) as being anticipated by *Yan* be withdrawn.

CONCLUSION

In view of the above amendment and remarks, Applicants respectfully assert that the rejection of the claims as set forth in the Office Action has been addressed and overcome. Applicants further respectfully assert that all claims are in condition for allowance and requests that an early notice of allowance be issued. If issues may be resolved through Examiner's Amendment, or clarified in any manner, a call to the undersigned attorney at (404) 879-2433 is respectfully requested.

No fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required, or credit any overpayment to Deposit Account No. 09-0528.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Jeffery B. Arnold', is written over a horizontal line.

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